

The Role of Fine Needle Aspiration Cytology (FNAC) in the Diagnosis of Thyroid Lesions

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The aim of this study was to evaluate the role of Fine Needle Aspiration Biopsy (FNAB) in the pre-operative diagnostic management of patients with solitary or dominant thyroid nodules. Fine Needle Aspiration Biopsy (FNAB) of the thyroid was performed on 632 patients referred to the Department of Pathology, King Edward Medical College. Out of the total of 632 aspirations performed, 532 (84.17%) were classified as benign. Colloid goitres/ Cysts/ Colloid nodules were the dominant benign lesion accounting for 479 (75.79%) cases. Other benign lesions included 45 (7.11%) adenomas and 8 (1.26%) cases of thyroiditis. 35 (5.53%) aspirates were included in the suspicious category and excisional biopsy was advised. Malignant lesions numbered 28 (4.43%), out of which Papillary carcinoma was the commonest malignancy diagnosed (42.8% of the thyroid cancers). 37 (5.85%) aspirates were considered inadequate for diagnostic evaluation. Results were tabulated and compared with other similar studies.

Keywords: Fine Needle Aspiration Cytology (FNAC), Thyroid, goitre, carcinoma, nodules.

Thyroid nodules either single or multiple are present in 4-7% of the adult population¹. They are a source of concern for the patients and a diagnostic dilemma for physicians². These nodules may be due to a variety of pathologic conditions both neoplastic and non neoplastic. Several diagnostic modalities such as the scintiscan, thyroid function tests and ultrasound have all been used recently; however none of them is absolutely diagnostic and only help to detect "cold nodules"³. A small proportion of cold nodules are undoubtedly malignant: a malignancy rate of 3% to 6% is usually found in an unselected series of patients with cold nodules who undergo surgery⁴. However, most thyroid nodules are benign, and it is difficult to exclude malignancy without excision and histological examination. The cost/benefit ratio makes it inadvisable to surgically remove all cold nodules and suggests a need for a pre-operative selection and evaluation of these patients⁵.

Fine Needle Aspiration Biopsy (FNAB) or Cytology (FNAC) has revolutionized the diagnostic approach in recent years and is being widely used as the initial diagnostic modality in identifying malignant nodules and selecting patients for surgery^{6,7}. Thus the critical issue is to determine whether the thyroid nodule is benign or malignant. The discovery of a malignant thyroid nodule on aspiration would necessitate a primary surgical therapy, whereas a benign nodule could be easily managed medically⁸.

ASPIRATION CYTOLOGY is a technique whereby small amounts of fluid, blood, cells and tissue fragments are obtained using a fine needle (22-25 gauge) and syringe⁹. The history of Fine Needle Aspiration dates back to the late 18th century but the first organized attempts at aspiration were made by Martin and Ellis in the period between 1926-1930 using 18 gauge needles¹⁰. By 1934, they had reported about 1400 positive diagnosis on aspirations¹¹. Swedish investigators, however were credited with demonstrating the merits of fine needle

aspiration Biopsy (FNAB) as a reliable tool in the diagnosis of benign and malignant thyroid nodules¹². Since then FNAC is being used increasingly for diagnosing numerous benign and malignant conditions and it has become a well accepted procedure for the diagnosis and management of breast masses, cold thyroid nodules, lymphadenopathies and soft tissue lesions¹³. It is recognized as a sensitive screening test that yields correct diagnosis in a higher percentage of cases at the lowest possible cost and in a remarkable short time^{14,15}.

Materials and Methods

From January 1999 to December 1999, a total of 632 FNAB'S were performed on the thyroid glands of patients presenting with a diffuse or nodular thyroid enlargement and solitary thyroid nodules. These patients were referred to the Department of Pathology, King Edward Medical College, Lahore, by the Out-patients Department of Mayo Hospital and some admitted patients were referred by the four Surgical Units of Mayo Hospital.

Some of these patients already had, had their thyroid scans, Thyroid functions tests and radioactive I-131 uptake done prior to the aspiration. Before performing the actual procedure of aspiration biopsy, physical examination of the thyroid gland was carried out to note its mobility during deglutition, its nodularity and evidence of any toxicosis by taking a thorough history. The cervical lymph nodes were also palpated for enlargement.

A 10- ml disposable plastic syringe (B D/ Nipro) with disposable fine needles of 22-23 gauges were used for all routine aspirations. The procedure was repeated two to three times from different areas of the gland and multiple smears were made on glass slides. In case of cystic nodules, the cyst contents were evacuated completely.

Some of the smears were fixed immediately in 95% alcohol and stained with Eosin Haematoxylin stain, whereas some were air dried and stained with Giemsa stain.

The parameters considered for the detailed cytologic assessment included the presence of follicular epithelial cells, colloid content, follicle (acinar) formation, haemosiderin laden macrophages, Hurthle cells, inflammatory cells like lymphocytes, plasma cells, lympho-histiocytic aggregates, papillary formations, intranuclear cytoplasmic inclusions, nuclear grooves and multinucleated giant cells¹⁶. An FNA sample was considered to be adequate if a minimum of 6 clusters of benign follicular cells in at least 2 slides prepared from separate aspirates were present³. A sample containing abundant colloid with occasional follicular cells was also considered adequate as this pattern was encountered in colloid cysts and in colloid goitres. Specimens with either no diagnostic cellular material or insufficient cells for a cytologic diagnosis were classified as Inadequate, and repeat aspiration was advised.

Results

Out of a total of 632 thyroid aspirates performed at the Department of Pathology, Kind Edward Medical College in the year 1999, there were 548 female and 54 male patients, giving a male: female ratio of 1: 10. The ages of these patients ranged from 14 years to 80 years. There were 595 adequate aspirates and 37 inadequate aspirates, as determined by the criteria already laid down in materials and the methods.

Table 1 and the Table 2 show the results of fine needle aspiration cytologic diagnosis in 632 cases. Of the lesions, 532 (84.17%) were classified as benign, 35 (5.53%) were suspicious, 28 (4.83%) were malignant and 37 (5.85%) were inadequate for a cytologic diagnosis.

The most common benign thyroid lesions reported on aspiration were Colloid goitres/ Colloid nodules/ Colloid cysts, which collectively accounted for 479 (75.79%) cases. The criteria used in the diagnosis was the presence of abundant colloid either gross or microscopic, follicular cells arranged in monolayered sheets or dispersed and the presence of many haemosiderin laden macrophages. The 3 cases of recurrent goitre included in our figure gave a history/ surgical scar of a previous subtotal thyroidectomy performed some years ago.

Other benign lesions reported in our study included 43 cases (6.80%) of Follicular Adenoma, out of which 20 cases were confirmed histologically, 5 turned out to be colloid goitres with areas of functional hyperactivity and the remaining 18 cases were lost to follow up. There were 2 cases of Hurthle cell adenoma in our study and both were confirmed on histological follow up. In addition we reported 8 cases of thyroiditis which included 3 cases of Hashimotos thyroiditis, 3 of giant cell thyroiditis and 2 cases of lymphocytic thyroiditis.

In the suspicious category we reported 35 cases (5.53%) of Follicular/Hurthle cell neoplasm, based on the morphologic criteria of hypercellularity, scant colloid background and nuclear pleomorphism. Out of these, surgical follow-up was available in only 12 cases, 2 turned

out to be Follicular adenomas, 4 were hyperplastic nodules, 1 was a Hurthle cell adenoma, 2 cases were of Follicular carcinoma and 3 cases were of Papillary Carcinoma.

Of the 28 malignant thyroid aspirates in our study, Papillary carcinoma was the commonest malignancy reported (Table 3). It accounted for 12 cases (42.85% of thyroid malignancies in our study). These included 10 females and 2 males giving a female: male ratio of 5:1. The second commonest malignancy reported was Anaplastic Cancer. It accounted for 9 cases (32.14% of thyroid malignancy). These included 4 female and 5 male patients in the age range of 30 to 70 years.

In addition we reported 2 cases of Follicular carcinoma (7.1%), 2 cases of Medullary Carcinoma (7.1%), 2 cases of Lymphoma (7.1%) and 1 case of a Metastatic lesion to the thyroid (3.57%) from a Poorly Differentiated Carcinoma of the Caecum.

No major complications were encountered following aspiration. Minor complications in the form of pain, ecchymosis, penetration into the trachea and fainting were rarely observed.

Table 1. Results of cytologically adequate thyroid aspirates (n=595) at K.E.M.C. in the year 1999

Category	No. of Cases	%age
Benign lesions	532	89.41
Suspicious lesions	35	5.88
Malignant	28	4.70
Total	595	100

Table 2. Results of FNA Cytology of the thyroid in 632 patients performed in the year 1999

Category	Diagnosis	No. of Pts.	%age	
Benign lesions	Colloid goitre	191	30.22	
	Colloid goitre with cystic change	39	6.17	
	Colloid cysts	90	14.24	
	Colloid nodules	156	24.68	
	Recurrent goitre	03	0.47	
	Follicular adenoma	43	6.80	
	Hurthle cell adenoma	02	0.31	
	Thyroiditis	8	1.26	
	Suspicious lesions		35	5.53
Malignant lesions	Follicular/ Hurthle cell neoplasm	35	5.53	
	Papillary carcinoma	12	1.89	
	Anaplastic carcinoma	9	1.42	
	Follicular carcinoma	2	0.31	
	Medullary carcinoma	2	0.31	
	Lymphoma	2	0.31	
	Metastatic deposits	1	0.15	
	Inadequate	Unsatisfactory samples	37	5.85
	Total		632	100

Table 3. Results of malignant thyroid aspirates (n=28)

Type of thyroid cancer	No. of Cases	%age
Papillary carcinoma	12	42.85
Anaplastic carcinoma	9	32.14
Follicular carcinoma	2	7.14
Medullary carcinoma	2	7.14
Lymphoma	2	7.14
Metastatic carcinoma	1	3.57
Total	28	100

Discussion

Preoperative FNAC used for the evaluation of thyroid nodules has become a standard practice in many institutions in screening and selecting patients for surgery^{14, 16}. In this regard FNA has been shown to be superior to Ultrasound and radionucleotide scanning¹⁷. The major advantages of the procedure are a reduction in the number of patients referred for surgical treatment and an increase in the yield of malignant neoplasms in those who are selected for surgery^{14, 18, 19}. According to Crile and Hawk⁶, aspiration biopsy will reduce the need for thyroidectomy in patients with small thyroid nodules by a factor of ten to one. Using FNA as the initial diagnostic modality the percentage of patients undergoing thyroidectomy has decreased by 25%, while the yield of cancer in surgically excised thyroids has increased from 15% to at least 30%^{4, 20}.

The main limitation of FNA is the occurrence of some inadequate aspirates. However it can be repeated in such cases without any risk to the patient. In our study we encountered 37 (5.85%) unsatisfactory aspirates. The incidence of inadequate samples in various studies has ranged from zero to as high as 25%^{5,12, 21, 22, 23}. A high incidence of inadequate samples is usually encountered when the cytopathologist who makes the diagnosis does not perform the aspiration himself and thus cannot judge the specimen adequacy at the time of the procedure²².

Non neoplastic benign lesions seen in our study were mainly colloid goitres, colloid nodules and thyroid cysts. Collectively these lesions accounted for 479 (75.79%) cases out of the total 632 aspirates. This result is in accordance to the figures of some other pathologists in Pakistan^{21, 23, 24} who give their figures as 75%, 81.18% and 73% respectively. Mandreker et al of India²² gives a 73% incidence of these benign thyroid lesions. The figures cited above are much higher than some other studies who give an incidence of these lesions in the range of 40% to 65%^{3,6}.

According to Deshpande et al²⁰, the term "follicular neoplasm" has been used in FNA diagnosis to include hyperplastic nodules, follicular adenomas and follicular carcinomas due to the difficulty in segregating the three lesions in FNA cytology. We deviated from his definition and attempted to diagnose follicular adenomas on cytologic patterns. We reported 43 follicular adenomas (6.80%) and based our criteria on the presence of hypercellular smears, uniform bland looking follicular cells arranged in acinar pattern, some Hurthle cell change and scant colloid material in the background and suggested

a surgical biopsy. Out of these, 20 cases were confirmed histologically as follicular adenomas, 5 were reported as hyperplastic nodules whereas 18 cases were lost to follow up. In addition we reported 2 cases of Hurthle cell adenoma on FNA and both were confirmed histologically.

Generally speaking, 10 to 30% of all thyroid FNA's are reported as suspicious²². This is a problem inherent in FNA of the thyroid because the diagnosis of Hurthle cell carcinoma and follicular carcinoma depends on the histologic criteria of vascular and capsular invasion, rather than on cytologic criteria, and there are no reliable criteria that can distinguish them from adenoma at the cellular level^{7,19}. It is therefore recommended that these lesions be grouped under the term "follicular neoplasm"²⁰. We reported 35 (5.53%) cases of follicular neoplasm based on the cytologic criteria of scanty colloid, hypercellularity, disarray of the follicular cells, papillae formation and moderate to severe pleomorphism. These figures are in close proximity to some other studies who give figures of 7.69%²¹, 7.58%²² and 4.78%²³. Out of these 35 cases only 10 were available for surgical biopsy; 5 were reported as adenomas, 2 as hyperplastic nodules, 2 as Papillary carcinoma and 1 as Follicular carcinoma showing both vascular and capsular invasion. The other 25 cases were lost to follow up.

Papillary Carcinoma is the most common histological subtype of thyroid malignancy accounting for 60-80% of all thyroid cancers^{18,25,26}. It may be discovered incidently during routine histological section of the thyroid, has a high tendency to metastasize to the cervical lymph nodes and in fact these enlarged lymph nodes are often the only manifestation of this malignancy^{26,27}. In our study Papillary carcinoma was also the commonest thyroid malignancy accounting for 42.85% of thyroid cancers. Studies by other workers^{19,21,22,24} on thyroid aspirates give an incidence in the range of 53-73% of Papillary carcinoma. In this group we had 2 cases in which FNA was primarily performed for cervical lymphadenopathy. Aspirates showed well-formed papillary fronds with fibrovascular cores and epithelial cell clusters with nuclear grooves and inclusions. A suspicion of Metastatic Papillary Thyroid Carcinoma was raised which was subsequently confirmed on thyroid aspiration and histology.

Anaplastic thyroid cancer is one of the most malignant tumours affecting humans. It is rare and constitutes 5-10% of thyroid malignancies^{26,28,29}. In our study it constituted 32.14% and was the second common malignancy whereas in other studies it accounted for 14.3%²¹ and 14.28%²⁴ respectively, which is about half the percentage observed in our study.

The two cases of Follicular carcinoma in our study had been previously reported on histopathology. One case presented with a recurrent thyroid nodule and previous surgical biopsy report showed Follicular carcinoma with cervical lymph node infiltration. The other case presented with a biopsy report of Metastatic Thyroid Follicular Carcinoma to the right parietal lobe of the brain. FNA

thyroid showed pleomorphic follicular cells and the case was reported as primary Follicular Carcinoma Thyroid. In our study the % of this malignancy was 7.14% as compared to other studies which show an incidence of 4% to 22%^{20,22}.

Medullary carcinoma accounts for 10% of all thyroid malignancies^{1,30}. Mandrekar et al²² give a 3.33% incidence of this malignancy in their study. Our study however gives a figure of 7.14%, same as for Follicular carcinoma and lymphoma.

Malignant lymphoma may involve the thyroid secondarily to systemic disease or it may develop as a primary thyroid neoplasm. Less than 5% of thyroid malignancies are primary lymphomas^{1,26} and 75% cases occur in relation to Hashimoto's thyroiditis²⁶. (In our study it comprised 7.14% of thyroid cancers. Both cases were secondary to Large Cell Lymphoma.

Metastatic cancer constitutes an uncommon thyroid malignancy^{1,26}. We reported a single case of Metastatic Poorly Differentiated Carcinoma Caecum based on previous history which was subsequently confirmed on histology.

We conclude that the procedure of FNAB allows the patient to remain an out-patient and avoids unnecessary hospitalization and surgical expenditure.

References

1. Robbins S.L, Kumar V.K, Cotran R.S. Robbins, Pathologic Basis of Disease. 5th Edition. W.B.Saunders Company (1994).
2. Hall T.L, Layfield L.J, Phillippe A, Rosenthal D.L. Sources of diagnostic error in fine needle aspiration of the thyroid. *Cancer* 1989; 63:718-725.
3. Pinto M.R, Mathew M. Fine needle aspiration and frozen section diagnosis in the management of thyroid nodules. *Annals of Saudi Medicine*.1995; 15:614-618.
4. Gharib H, Goellner J, R. Fine needle aspiration biopsy of the thyroid: An appraisal. *Ann. of Internal Medicine*.1993;118:282-290.
5. La Rosa G.L, Belfiore A, Giuffrida D, Sicurella C. Evaluation of the fine needle aspiration biopsy in the preoperative selection of cold thyroid nodules. *Cancer*,1991;67:2137-2141.
6. Crile G, Hawk W.A. Aspiration biopsy of thyroid, *Surg Gynae and Obs*.1973;136:241-245.
7. Cusick E.L, Macintosh C.A, Krukowski Z.H, Williams M.M. Management of isolated thyroid swellings: a prospective six year study of fine needle aspiration cytology in diagnosis. *B.M J*; 303:318-321.
8. Ridgway E.C, Clinical Review 30. Clinician's evaluation of a solitary thyroid nodule. *Journal of Clinical Endocrinology and Metabolism*. 1992; 74:231-233.
9. Linsk J.A, Franzen S. Fine needle aspiration for the clinician. 2nd Edition. Philadelphia. J.B.Lippincott Company 1981.
10. Martin H.E, Ellis E.B. Biopsy by needle puncture and aspiration. *Annals of Surgery*, 1930; 92: 169-181.
11. Martin H.E, Ellis E.B. Aspiration biopsy. *Surgery Gynae and Obs* 1934, 59: 578-589.
12. Mac Donald L, Yazdi H.M. Non diagnostic fine needle aspiration Biopsy of the thyroid gland. *Acta Cytologica* 1996; 40:423-428.
13. Layfield L.J, Anders K.H, Glasgow B.J, Mirra J.M. Fine needle aspiration of primary soft tissue lesions. *Arch. Path. Lab Medicine* 1986; 110: 420-426.
14. Ashraf A.A, Akhtar M, Woodhouse N. Aspiration Biopsy of thyroid nodules. A review of the experience at KFS Hospital. *Annals of Saudi Medicine*. 1986; 6:163-171.
15. Frable M.A.S and Frable W.J. Fine needle aspiration biopsy revisited. *Laryngoscope*. 1982; 92:1414-1418.
16. Das D.K, Khanna C.M, Tripathi R.P, Pant C.S, Mandal A.K. Solitary nodular goitre: Review of cytomorphologic features in 441 cases. *Acta Cytologica* 1999; 43: 563-574.
17. Layfield L.J, Mohrman R.L, Kopald K.H, Giuliano A.E. Use of aspiration cytology and frozen section examination for management of benign and malignant thyroid nodules. *Cancer* 1991; 68: 130-134.
18. Oertel Y.C, Oertel J.E. Diagnosis of malignant epithelial thyroid lesions: fine needle aspiration and histopathologic correlation. *Ann. Diag. Pathology*. 1998; 2(6): 377-400.
19. Rosen Y, Rosenblatt P, Saltzman E. Intra operative pathologic diagnosis of thyroid neoplasm. Report on experience with 504 specimens. *Cancer* 1990; 66: 2001-2006.
20. Deshpande V, Kapila K, Siva Sai K, Verma K. Follicular neoplasms of the thyroid. Decision tree approach using morphologic and morphometric parameters. *Acta Cyto* 1997; 41: 369-376.
21. Chughtai A.S, Khalil M.E, Rashid A, Chughtai R.S, Malik N. A, Nagi A.H. Fine needle aspiration cytology in the diagnosis of palpable thyroid lesions. *Pakistan J. of Surgery*. 1996; 12: 88-90.
22. Mandrekar S.R.S, Nadkarni N.S, Pinto R.G.W, Menezes S. Role of fine needle aspiration cytology as the initial modality in the investigations of thyroid lesions. *Acta Cyto* 1995; 39: 898-904.
23. Kamal F, Niazi S, Nagi A.H, Al Jaradi M, Naveed I.A. Fine needle aspiration cytology: an experience at King Edward Medical College Lahore, Pakistan. *Journal of Path.*1996; 7(1): 33-36.
24. Aslam M. Fine needle aspiration cytology. Role in thyroid swellings. *The Professional* 1999, 06: 353-358.
25. Rosai J, Zampi G, Carcani M, L. Papillary carcinoma of the thyroid, a discussion of its several morphologic expressions with particular emphasis on the follicular variant. *Am. J. of Surg.Path.* 1983; 7: 809-817.
26. Orell S.R, Philips J. The thyroid. Fine needle and cytologic diagnosis of thyroid lesions 1997. Karger Press. Chapter 7. Cytological patterns in Thyroid disease. 61-199.
27. Bramley M.D and Bramley B.J. Papillary microcarcinoma of the thyroid gland. *British Journal of Surgery* 1996; 83: 1674-1683.
28. Us- Krasovec M, Golouh R, Marija A, Besic N, Oblak L.R. Anaplastic Thyroid Carcinoma in Fine needle aspirates. *Acta Cyto* 1996; 40: 953-958.
29. Kumar P.V, Torabinejad S, Omrani G.H. Osteoclastomalike Anaplastic carcinoma of the thyroid gland diagnosed by FNAC. *Acta Cyto* 1997; 41, 1345-1348.
30. Collins B.T, Cramer H.H, Tabatowski K, Hearn S, Raminhos A, Lampse H. Fine needle aspiration of Medullary carcinoma of the thyroid. *Acta Cyto* 1994, Vol: 39, 920-930.